

CLAIMS

1. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1, an immunogenic fragment of the Pseudo-ICE, or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1 $\beta$  secretion, and stimulating NF- $\kappa$ B activation.
2. The isolated nucleic acid molecule of claim 1 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.
3. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid sequence has a nucleotide sequence at least 98% identical to SEQ ID NO:2.
4. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid sequence has a nucleotide sequence as set forth in SEQ ID NO:2.
5. A nucleic acid vector comprising a nucleic acid sequence encoding a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE.
6. The nucleic acid vector of claim 5 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.
7. The nucleic acid vector of claim 5 wherein the nucleic acid sequence has a nucleotide sequence at least 98% identical to SEQ ID NO:2.
8. The nucleic acid vector of claim 5 wherein the nucleic acid sequence has a nucleotide sequence as set forth in SEQ ID NO:2.

9. A host cell containing the nucleic acid vector of claim 5.
10. The host cell of claim 9 wherein the host cell is selected from the group consisting of a mammalian cell, a plant cell, an insect cell, a yeast cell and a bacterial cell.
11. An isolated polypeptide comprising a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1, an immunogenic fragment of the Pseudo-ICE, or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1 $\beta$  secretion, and stimulating NF- $\kappa$ B activation.
12. The isolated polypeptide of claim 11 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.
13. An isolated polypeptide encoded by a nucleotide sequence at least 98% identical to SEQ ID NO:2 and having an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1 $\beta$  secretion, and stimulating NF- $\kappa$ B activation.
14. An antibody comprising an immunoglobulin or antigen-binding fragment thereof that specifically binds the isolated polypeptide of claim 11 or claim 12.
15. A composition comprising the isolated polypeptide of claim 11 or claim 12 and a physiologically acceptable carrier.
16. A method of transforming or transfecting a cell with a nucleic acid molecule encoding a Pseudo-ICE that has at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1 $\beta$  secretion, and stimulating NF-

$\kappa$ B activation, comprising contacting the cell with a vector comprising the nucleic acid molecule under the control of a promoter.

17. The method of claim 16 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.

18. The method of claim 16 wherein the nucleic acid molecule is at least 98% identical to SEQ ID NO:2.

19. The method of claim 16 wherein the nucleic acid molecule has a nucleotide sequence set forth in SEQ ID NO:2.

20. The method of claim 16 wherein the nucleic acid molecule is in the sense orientation with respect to the promoter.

21. The method of claim 16 wherein the nucleic acid molecule is in the antisense orientation with respect to the promoter.

22. A method of inhibiting apoptosis or inflammation comprising contacting a cell expressing a pro-caspase-1 with a composition comprising the isolated polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the inhibition of apoptosis.

23. A method of inhibiting apoptosis or inflammation comprising contacting a cell expressing a pro-caspase-1 with a composition comprising the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the inhibition of apoptosis.

24. A method of stimulating apoptosis comprising contacting a cell expressing a pro-caspase-1 a composition comprising a polypeptide that specifically binds to the isolated

polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the stimulation of apoptosis.

25. The method of claim 24 wherein the polypeptide is an immunoglobulin or antigen-binding fragment thereof that specifically binds to the isolated polypeptide of claim 11 or claim 12.

26. A method of stimulating apoptosis comprising contacting a cell expressing a pro-caspase-1 a composition comprising an antisense or ribozyme construct of the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the stimulation of apoptosis.

27. A method of inhibiting the activation of a pro-caspase-1 comprising contacting a cell expressing the pro-caspase-1 with a composition comprising the isolated polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the inhibition of the activation of the pro-caspase-1.

28. A method of inhibiting the activation of a pro-caspase-1 comprising contacting a cell expressing the pro-caspase-1 with a composition comprising the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the inhibition of the activation of the pro-caspase-1.

29. A method of stimulating the activation of a pro-caspase-1 comprising contacting a cell expressing the pro-caspase-1 a composition comprising a polypeptide that specifically binds to the isolated polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the stimulation of the activation of the pro-caspase-1.

30. The method of claim 29 wherein the polypeptide is an immunoglobulin or antigen-binding fragment thereof that specifically binds to the isolated polypeptide of claim 11 or claim 12.

31. A method of stimulating the activation of a pro-caspase-1 comprising contacting a cell expressing the pro-caspase-1 a composition comprising an antisense or ribozyme construct of the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the stimulation of the activation of the pro-caspase-1.

32. A method of identifying inhibitors or enhancers of Pseudo-ICE mediated inhibition of pro-caspase-1 activation, comprising:

a. contacting a cell transfected with an expression vector encoding Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE capable of inhibiting pro-caspase-1 activation with a candidate inhibitor or enhancer; and

b. detecting an increase or decrease in pro-caspase-1 activation in the presence of the candidate inhibitor or enhancer, wherein a decrease in pro-caspase-1 activation indicates the presence of an enhancer of Pseudo-ICE mediated inhibition of pro-caspase-1 activation and an increase in pro-caspase-1 activation indicates the presence of an enhancer.

33. The method of claim 32 wherein step (b) detects the level of pro-caspase-1 oligomerization.

34. The method of claim 32 wherein step (b) detects the level of the pro-caspase-1 processing activity.

35. The method of claim 32 wherein step (b) detects the substrate cleavage activity of the caspase-1 processed from the pro-caspase-1.

36. The method of claim 32 wherein step (b) detects the level of IL-1 $\beta$  secretion induced by an inflammatory stimulus.

37. A method of inhibiting induced secretion of IL-1 $\beta$  comprising contacting a cell subject to an inflammatory stimulus that induces IL-1 $\beta$  secretion with a composition comprising the isolated polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the inhibition of IL-1 $\beta$  secretion induced by the stimulus.

38. A method of inhibiting induced secretion of IL-1 $\beta$  comprising contacting a cell subject to an inflammatory stimulus that induces IL-1 $\beta$  secretion with a composition comprising the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the inhibition of IL-1 $\beta$  secretion induced by the stimulus.

39. The method of claim 37 or claim 38 wherein the inflammatory stimulus is an IFN- $\gamma$ , a TNF, or a lipopolysaccharide.

40. A method of identifying inhibitors or enhancers of Pseudo-ICE mediated inhibition of IL-1 $\beta$  secretion in response to an inflammatory stimulus, comprising:

- a. contacting a cell transfected with an expression vector encoding Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE capable of inhibiting the IL-1 $\beta$  secretion with a candidate inhibitor or enhancer;
- b. subjecting the transfected cell to an inflammatory stimulus; and
- c. detecting an increase or decrease in the IL-1 $\beta$  secretion level induced by the inflammatory stimulus in the presence of the candidate inhibitor or enhancer, wherein a decrease in the induced IL-1 $\beta$  secretion indicates the presence of an enhancer of Pseudo-ICE mediated inhibition of the induced IL-1 $\beta$  secretion and an increase in the induced IL-1 $\beta$  secretion indicates the presence of an inhibitor of Pseudo-ICE mediated inhibition of the induced IL-1 $\beta$  secretion.

41. The method of claim 40 wherein the inflammatory stimulus is an IFN- $\gamma$ , a TNF, or a lipopolysaccharide.

42. The method of claim 30 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.

43. A method of stimulating the activation of an NF-kB comprising contacting a cell expressing the NF-kB with a composition comprising the isolated polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the inhibition of the activation of the NF-kB.

44. A method of stimulating the activation of an NF-kB comprising contacting a cell expressing the NF-kB with a composition comprising the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the inhibition of the activation of the NF-kB.

45. A method of inhibiting the activation of an NF-kB comprising contacting a cell expressing the NF-kB a composition comprising a polypeptide that specifically binds to the isolated polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the stimulation of the activation of the NF-kB.

46. The method of claim 45 wherein the polypeptide is an immunoglobulin or antigen-binding fragment thereof that specifically binds to the isolated polypeptide of claim 11 or claim 10.

47. A method of inhibiting the activation of an NF-kB comprising contacting a cell expressing the NF-kB a composition comprising an antisense or ribozyme construct of the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the stimulation of the activation of the NF-kB.

48. A method of identifying inhibitors or enhancers of Pseudo-ICE mediated NF-κB activation, comprising:

a. contacting a cell transfected with an expression vector encoding Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE capable of stimulating NF-κB activation with a candidate inhibitor or enhancer; and

b. detecting an increase or decrease in NF-κB activation in the presence of the candidate inhibitor or enhancer, wherein a decrease in NF-κB activation indicates the presence of an inhibitor and an increase in NF-κB indicates the presence of an enhancer.

49. The method of claim 48 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.

50. A method of identifying a polypeptide that specifically binds to a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1 $\beta$  secretion, and stimulating NF-κB activation, comprising:

a. contacting a sample with the Pseudo-ICE or the functional fragment under conditions that permit the formation of a complex between the Pseudo-ICE or the functional fragment thereof and the polypeptide; and

b. detecting the complex and polypeptide in the complex.

51. The method of claim 50 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.

52. The method of claim 50 wherein the Pseudo-ICE or the functional fragment thereof is covalently bound to a detectable moiety.

53. The method of claim 52 wherein the detectable moiety is a reporter molecule.

54. The method of claim 52 wherein the detectable moiety is a radionuclide.

55. The method of claim 50 wherein the sample comprises a cDNA expression library.

56. A nucleic acid molecule comprising a first nucleic acid sequence encoding a Pseudo-ICE having at least 80% identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1 $\beta$  secretion, and stimulating NF- $\kappa$ B activation and a second nucleic acid sequence encoding the transcription activation domain or the DNA-binding domain of a transcription factor.

57. A method for identifying a polypeptide that specifically binds to a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1 $\beta$  secretion, and stimulating NF- $\kappa$ B activation with a yeast two-hybrid screening system, comprising transforming a yeast cell with a vector comprising the nucleic acid molecule of claim 56.

58. A method for identifying a compound that increases the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of Pseudo-ICE capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

a. combining the Pseudo-ICE or the functional fragment with the pro-caspase-1 or the fragment thereof in the absence of a candidate compound under conditions that

allow specific binding between the Pseudo-ICE or the functional fragment and the pro-caspase-1 or the fragment thereof;

b. combining the Pseudo-ICE or the functional fragment with the pro-caspase-1 or the fragment thereof in the presence of the candidate compound under conditions of step (a);

c. comparing the specific binding between the Pseudo-ICE or the functional fragment and the pro-caspase-1 or the fragment thereof of step (a) with that of step (b) to thereby determine whether the candidate compound is capable of increasing the specific binding between the Pseudo-ICE or the functional fragment and the pro-caspase-1 or the fragment thereof.

59. The method of claim 58 wherein the Pseudo-ICE has an amino acid sequence of SEQ ID NO:1.

60. A process for manufacturing a compound that increases the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of Pseudo-ICE capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

a. carrying out the method of claim 58 to identify a compound that increases the specific binding between a pro-caspase-1 or a fragment thereof and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of Pseudo-ICE capable of binding to the pro-caspase-1;

b. derivatizing the compound; and

c. optionally repeating steps a and b.

61. The process of claim 60 wherein the Pseudo-ICE has an amino acid sequence of SEQ ID NO:1.

62. A method for identifying a compound that decreases the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of Pseudo-ICE capable of binding to a pro-caspase-1, comprising:

a. combining the Pseudo-ICE or the functional fragment with the pro-caspase-1 in the absence of a candidate compound under conditions that allow specific binding between the Pseudo-ICE or the functional fragment and the pro-caspase-1 or the fragment thereof;

b. combining the Pseudo-ICE or the functional fragment with the pro-caspase-1 or the fragment thereof in the presence of the candidate compound under conditions of step (a); and

c. comparing the specific binding between the Pseudo-ICE or the functional fragment and the pro-caspase-1 or the fragment thereof of step (a) with that of step (b) to thereby determine whether the candidate compound is capable of decreasing the specific binding between the Pseudo-ICE or the functional fragment and the pro-caspase-1.

63. The method of claim 62 wherein the Pseudo-ICE has an amino acid sequence of SEQ ID NO:1.

64. A process for manufacturing a compound that decreases the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of Pseudo-ICE capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

a. carrying out the method of claim 48 to identify a compound that decreases the specific binding between the pro-caspase-1 or the fragment thereof and the Pseudo-ICE or the functional fragment of Pseudo-ICE;

- b. derivatizing the compound; and
- c. optionally repeating steps a and b.

65. The process of claim 64 wherein the Pseudo-ICE has an amino acid sequence of SEQ ID NO:1.

66. A method for identifying a compound that disrupts the binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

a. contacting a candidate compound with a binding complex comprising the Pseudo-ICE or the functional fragment and the pro-caspase-1; and

b. detecting the Pseudo-ICE, the functional fragment, the pro-caspase-1 or the fragment thereof that dissociates from the binding complex to thereby determine whether the candidate compound is capable of disrupting the binding between the pro-caspase-1 or the fragment thereof and the Pseudo-ICE or the functional fragment.

67. The method of claim 66 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.

68. The method of claim 66 wherein the Pseudo-ICE, the functional fragment, the pro-caspase-1 or the fragment thereof is covalently bound to a detectable moiety.

69. The method of claim 68 wherein the detectable moiety is a reporter molecule.

70. The method of claim 68 wherein the detectable moiety is radionuclide.

71. A process for manufacturing a compound that disrupts the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional

fragment of Pseudo-ICE capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

- a. carrying out the method of claim 66 to identify a compound that disrupts the specific binding between the pro-caspase-1 or the fragment thereof and the Pseudo-ICE or the functional fragment of Pseudo-ICE;
- b. derivatizing the compound; and
- c. optionally repeating steps a and b.

72. The process of claim 71 wherein the Pseudo-ICE has an amino acid sequence of SEQ ID NO:1.

73. A method for identifying a compound that increases the specific binding between a RICK and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of Pseudo-ICE capable of binding to the RICK, comprising:

- a. combining the Pseudo-ICE or the functional fragment with the RICK in the absence of a candidate compound under conditions that allow specific binding between the Pseudo-ICE or the functional fragment and the caspase-1;
- b. combining the Pseudo-ICE or the functional fragment with the RICK in the presence of the candidate compound under conditions of step (a);
- c. comparing the specific binding between the Pseudo-ICE or the functional fragment and the RICK of step (a) with that of step (b) to thereby determine whether the candidate compound is capable of increasing the specific binding between the Pseudo-ICE or the functional fragment and the RICK.

74. The method of claim 73 wherein the Pseudo-ICE has an amino acid sequence of SEQ ID NO:1.

75. A method for identifying a compound that decreases the specific binding between a RICK and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of Pseudo-ICE capable of binding to a RICK, comprising:

a. combining the Pseudo-ICE or the functional fragment with the RICK in the absence of a candidate compound under conditions that allow specific binding between the Pseudo-ICE or the functional fragment and the RICK;

b. combining the Pseudo-ICE or the functional fragment with the RICK in the presence of the candidate compound under conditions of step (a); and

c. comparing the specific binding between the Pseudo-ICE or the functional fragment and the RICK of step (a) with that of step (b) to thereby determine whether the candidate compound is capable of decreasing the specific binding between the Pseudo-ICE or the functional fragment and the RICK.

76. The method of claim 75 wherein the Pseudo-ICE has an amino acid sequence of SEQ ID NO:1.

77. A method for identifying a compound that disrupts the binding between a RICK and a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO:1 or a functional fragment of the Pseudo-ICE capable of binding to the RICK, comprising:

a. contacting a candidate compound with a binding complex comprising the Pseudo-ICE or the functional fragment and the RICK; and

b. detecting the Pseudo-ICE, the functional fragment, or the RICK that dissociates from the binding complex to thereby determine whether the candidate compound is capable of disrupting the binding between the RICK and the Pseudo-ICE or the functional fragment.

78. The method of claim 77 wherein the Pseudo-ICE has an amino acid sequence set forth in SEQ ID NO:1.

79. The method of claim 77 wherein the Pseudo-ICE, the functional fragment or the RICK is covalently bound to a detectable moiety.

80. The method of claim 79 wherein the detectable moiety is a reporter molecule.

81. The method of claim 79 wherein the detectable moiety is radionuclide.

82. A method of identifying inhibitors or enhancers of ICE-Like mediated inhibition of pro-caspase-1 activation, comprising:

a. contacting a cell transfected with an expression vector encoding ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 (ICE-Like amino acid sequence) or a functional fragment of the ICE-Like capable of inhibiting pro-caspase-1 activation with a candidate inhibitor or enhancer; and

b. detecting an increase or decrease in pro-caspase-1 activation in the presence of the candidate inhibitor or enhancer, wherein a decrease in pro-caspase-1 activation indicates the presence of an enhancer of ICE-Like mediated inhibition of pro-caspase-1 activation and an increase in pro-caspase-1 activation indicates the presence of an inhibitor of ICE-Like mediated inhibition of pro-caspase-1 activation.

83. The method of claim 82 wherein step (b) detects the level of pro-caspase-1 oligomerization.

84. The method of claim 82 wherein step (b) detects the level of caspase processing activity.

85. The method of claim 82 wherein step (b) detects the substrate cleavage activity of the caspase-1 processed from the pro-caspase-1.

86. The method of claim 82 wherein step (b) detects the level of IL-1 $\beta$  secretion induced by an inflammatory stimulus.

87. The method of claim 86 wherein the inflammatory stimulus is a lipopolysaccharide, an IFN- $\gamma$ , or a TNF.

88. A method of identifying inhibitors or enhancers of ICE-Like mediated inhibition of the IL-1 $\beta$  secretion in response to an inflammatory stimulus, comprising:

- a. contacting a cell transfected with an expression vector encoding ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of the ICE-Like capable of inhibiting IL-1 $\beta$  secretion with a candidate inhibitor or enhancer;
- b. subjecting the transfected cell to an inflammatory stimulus; and
- c. detecting an increase or decrease in the IL-1 $\beta$  secretion level induced by the inflammatory stimulus in the presence of the candidate inhibitor or enhancer, wherein a decrease in the induced IL-1 $\beta$  secretion indicates the presence of an enhancer of ICE-Like mediated inhibition of the induced IL-1 $\beta$  secretion and an increase in the induced IL-1 $\beta$  secretion indicates the presence of an inhibitor of ICE-Like mediated inhibition of the induced IL-1 $\beta$  secretion.

89. The method of claim 88 wherein the inflammatory stimulus is an IFN- $\gamma$ , a TNF, or a lipopolysaccharide.

90. The method of claim 88 wherein the ICE-Like has an amino acid sequence set forth in SEQ ID NO:3.

91. A method of identifying a polypeptide that specifically binds to an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of the ICE-Like capable of specifically binding to pro-caspase-1 or inhibiting induced IL-1 $\beta$  secretion, comprising:

a. contacting a cDNA expression library with the ICE-Like or the functional fragment under conditions that permit the formation of a complex between the ICE-Like or the functional fragment thereof and a polypeptide encoded by a clone of the cDNA expression library; and

b. detecting the complex and the polypeptide in the complex.

92. The method of claim 91 wherein the ICE-Like has an amino acid sequence set forth in SEQ ID NO:3.

93. The method of claim 91 wherein the ICE-Like or the functional fragment thereof is covalently bound to a detectable moiety.

94. The method of claim 93 wherein the detectable moiety is a reporter molecule.

95. The method of claim 93 wherein the detectable moiety is a radionuclide.

96. A nucleic acid molecule comprising a first nucleic acid sequence encoding an ICE-Like having at least 80% identity to SEQ ID NO:3 or a functional fragment of the ICE-Like capable of specifically binding to pro-caspase-1 or inhibiting induced IL-1 $\beta$  secretion and a second nucleic acid sequence encoding the transcription activation domain or the DNA-binding domain of a transcription factor.

97. A method for identifying a polypeptide that specifically binds to an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of the

ICE-Like capable of specifically binding to pro-caspase-1 or inhibiting induced IL-1 $\beta$  secretion with a yeast two-hybrid screening system, comprising transforming a yeast cell with a vector comprising the nucleic acid molecule of claim 96.

98. A method for identifying a compound that increases the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pre-caspase-1 and an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of ICE-Like capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

a. combining the ICE-Like or the functional fragment with the pro-caspase-1 or the fragment thereof in the absence of a candidate compound under conditions that allow specific binding between the ICE-Like or the functional fragment and the caspase-1 or the fragment thereof;

b. combining the ICE-Like or the functional fragment with the pro-caspase-1 or the fragment thereof in the presence of the candidate compound under conditions of step (a); and

c. comparing the specific binding between the ICE-Like or the functional fragment and the pro-caspase-1 or the fragment thereof of step (a) with that of step (b) to thereby determine whether the candidate compound is capable of increasing the specific binding between the ICE-Like or the functional fragment and the pro-caspase-1.

99. The method of claim 98 wherein the ICE-Like has an amino acid sequence of SEQ ID NO:3.

100. A process for manufacturing a compound that increases the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of ICE-Like capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

- a. carrying out the method of claim 98 to identify a compound that increases the specific binding between the pro-caspase-1 or the fragment thereof and the ICE-Like or the functional fragment;
- b. derivatizing the compound; and
- c. optionally repeating steps a and b.

101. The process of claim 100 wherein the ICE-Like has an amino acid sequence of SEQ ID NO:3.

102. A method for identifying a compound that decreases the specific binding between a pro-caspase-1 and an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of ICE-Like capable of binding to a pro-caspase-1, comprising:

- a. combining the ICE-Like or the functional fragment with the pro-caspase-1 in the absence of a candidate compound under conditions that allow specific binding between the ICE-Like or the functional fragment and the caspase-1;
- b. combining the ICE-Like or the functional fragment with the pro-caspase-1 in the presence of the candidate compound under conditions of step (a);
- c. comparing the specific binding between the ICE-Like or the functional fragment and the pro-caspase-1 of step (a) with that of step (b) to thereby determine whether the candidate compound is capable of decreasing the specific binding between the ICE-Like or the functional fragment and the pro-caspase-1.

103. The method of claim 102 wherein the ICE-Like has an amino acid sequence of SEQ ID NO:3.

104. A process for manufacturing a compound that decreases the specific binding between a pro-caspase-1 and an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of ICE-Like capable of binding to the pro-caspase-1, comprising:

- a. carrying out the method of claim 102 to identify a compound that decreases the specific binding between the pro-caspase-1 and the ICE-Like or the functional fragment;
- b. derivatizing the compound; and
- c. optionally repeating steps a and b.

105. The process of claim 102 wherein the ICE-Like has an amino acid sequence of SEQ ID NO:3.

106. A method for identifying a compound that disrupts the binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of the ICE-Like capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

- a. contacting a candidate compound with a binding complex comprising the ICE-Like or the functional fragment and the pro-caspase-1 or the fragment thereof; and
- b. detecting the ICE-Like, the functional fragment, or the pro-caspase-1 or the fragment thereof that dissociates from the binding complex to thereby determine whether the candidate compound is capable of disrupting the binding between the pro-caspase-1 or the fragment thereof and the ICE-Like or the functional fragment.

107. The method of claim 106 wherein the ICE-Like has an amino acid sequence set forth in SEQ ID NO:1.

108. The method of claim 106 wherein the ICE-Like, the functional fragment, the pro-caspase-1 or the fragment thereof is covalently bound to a detectable moiety.

109. The method of claim 108 wherein the detectable moiety is a reporter molecule.

110. The method of claim 108 wherein the detectable moiety is radionuclide.

111. A process for manufacturing a compound that disrupts the specific binding between a pro-caspase-1 or a fragment thereof that comprises a pro-domain of the pro-caspase-1 and an ICE-Like having at least 80% amino acid identity to SEQ ID NO:3 or a functional fragment of ICE-Like capable of binding to the pro-caspase-1 or the fragment thereof, comprising:

- a. carrying out the method of claim 107 to identify a compound that disrupts the specific binding between the pro-caspase-1 or the fragment thereof and the ICE-Like or the functional fragment;
- b. derivatizing the compound; and
- c. optionally repeating steps a and b.

112. The process of claim 111 wherein the ICE-Like has an amino acid sequence of SEQ ID NO:3.